REMARKS

After entry of this amendment, claims 1-23 are pending. The claims have amended without prejudice or disclaimer and find support *inter alia* in the original claims. Claim 1 finds further support in the original claim 4 and in the specification, for example, at page 3, lines 16-24, and page 30, line 39, through page 31, line 19. No new matter has been added.

The above amendments further narrow the scope of the claims and thus, do not present any new issues that require further consideration or search. Accordingly, Applicants respectfully request entry of the above amendments as they are believed to put the claims in condition for allowance or, alternatively, in better form for consideration on appeal. Thus, entry under 37 CFR §1.116 is correct.

Claim Objections

Claims 2-3 and 12-13 are objected to for reciting non-elected sequences and claims 4-5 and 21 are rejected for reciting non-elected invention. Applicants respectfully disagree.

As noted by the Examiner previously, the restriction requirement between sequences is subject to non-allowance of the generic claims 1 and 2 and the restriction requirement between Groups I-V is also subject to non-allowance of the generic claim 1. Thus, in the event that claims 1 and 2 are found allowable, rejoinder of the non-elected subject matter that would depend from or otherwise include all the limitations of the allowed claim is respectfully requested. MPEP § 821.04(b). Upon allowance of the generic claims (claims 1 and 2) or the claims directed to the elected species, Applicants respectfully request rejoinder of the non-elected species. 37 CFR § 1.141; MPEP § 809.02(a).

Claim Rejections – 35 U.S.C. § 112

Claims 1-23 remain rejected for allegedly lacking an enabling disclosure and for allegedly failing to comply with the written description requirement. Applicants respectfully disagree and traverse the rejections. However, to expedite prosecution, the claims have been amended without prejudice or disclaimer to recite the claimed method with more specificity. Applicants respectfully submit that the claims as amended overcome both rejections for the reasons already of record and for the following reasons.

Enablement Rejection

Claims 1-23 remain rejected for alleged lack of an enabling disclosure.

It is noted initially that, without acquiescing to the merits of the Examiner's argument, claim 1 has been amended without prejudice or disclaimer to recite the claimed method with more specificity. As amended, claim 1 further specifies that the reduction of NADPH oxidase content/activity/function is achieved by an NADPH oxidase sense nucleic acid sequence, an NADPH oxidase antisense nucleic acid sequence, or a RNA interference (RNAi) approach using a NADPH oxidase nucleic acid sequence. Thus, the claimed method, as amended, uses NADPH oxidase nucleic acids in achieving the reduction of NADPH oxidase content/activity/function by sense, antisense, or RNA interference approach. Applicants believe that the present amendment clarifies the Examiner's concerns that the claims encompass any method of reducing NADPH oxidase content/activity/function using sequences or products other than NADPH oxidase nucleic acid sequences.

The Examiner further contends that, while the specification mentions that an antisense or sense suppression of SEQ ID NO: 1 can be used to reduce NADPH oxidase expression, the art concerning using sense or antisense technology to reduce endogenous gene expression is unpredictable, citing to Schiene *et al.* (hereinafter "Schiene") for support. Applicants respectfully disagree with the Examiner's characterization of Schiene and submit that Schiene does not support the position alleged by the Examiner. Rather, this reference supports enablement and show that down-regulation of gene expression using antisense was predictable as of, at the latest, the year of 2000.

For instance, as noted by the Examiner, Schiene discloses transgenic tobacco plants that express an antisense construct derived from an Alfalfa cDNA encoding a Rac-related small GTP-binding protein ("Ms-*rac1*"). In addition to transgenic tobacco plants expressing Ms-*rac1* in antisense orientation ("*rac1*-antisense plants"), transgenic tobacco plants expressing Ms-*rac1* in sense orientation ("*rac1*-sense plants") is also generated. As observed by Schiene, most of the *rac1*-sense plants produced a necrotic reaction after infiltrating with yeast elicitor as did in the control transgenic plants transformed with empty vector, which indicates the development of plant defense reactions. See Schiene at page 767, left Col., 1st paragraph, and Table 3, and page

768, right Col., lines 9-15. On the other hand, most of the *rac1*-antisense plants failed to show any reaction or necrotic lesions upon elicitation, which indicates that those plants were defective in the establishment of plant defense reactions. *Id.* It has been proposed that Rac-related proteins may be involved in the onset of the oxidation burst reaction, one of the earliest plant defense reactions after pathogen attack (e.g. infiltration with yeast elicitor). See Schiene at page 762, left Col., 1st paragraph. It would be, therefore, expected and predictable that, when the expression of a Rac-related protein is down-regulated by, for example, an antisense construct, the onset of the oxidation burst reaction would be affected resulting in defective defense reactions in such a plant. This is exactly what observed in Schiene, where *rac1*-antisense plants failed to show necrotic lesions, and thus defense reactions, upon infiltration with yeast elicitor. Such a result is likely because the onset of the oxidation burst reaction was blocked or affected by the down-regulation of the Rac-related protein due to the expression of *rac1*-antisense construct. Accordingly, Applicants respectfully submit that Schiene supports predictability of down-regulation of gene expression using antisense rather than unpredictability as alleged by the Examiner.

Moreover, Applicants further submit that Schiene does not support unpredictability of down-regulation of gene expression using sense co-suppression as alleged by the Examiner. As known to one skilled in the art, introduction of a sense construct generally leads to overexpression of the nucleic acid contained in such a construct. Under certain conditions when co-suppression occurs, down-regulation of the gene expression takes place. Conversely, introduction of an antisense construct always leads to down-regulation. The *rac1*-sense construct used in Schiene allows overexpression of the Rac-like protein since, as discussed above, Rac-related protein is associated with defense mechanism and most of the *rac1*-sense plants produced in Schiene developed plant defense reactions upon infiltration of yeast elicitor. Thus, it is clear that Schiene did not use the *rac1*-sense construct for the purposes of down-regulating the expression of a Rac-related protein. Rather, as also discussed above, the *rac1*-antisense construct was used for such purposes in Schiene. Because Schiene did not use and/or explore co-suppression using sense sequences, Schiene does not support the alleged unpredictability of using such a technology according to the Examiner.

To further support the allegation of unpredictability, the Examiner additionally argues that, "since NADPH oxidases are encodes by a multigene family, one of ordinary skill in the art would not expect that using an antisense or sense suppression methodology would inhibit or reduce NADPH oxidase activity in the plant." Office Action at page 5. Applicants respectfully disagree and wish to direct the Examiner's attention again to the cited Schiene reference. As disclosed in Schiene, Rac-like proteins belong to the superfamily of small GTP-binding proteins, which is also a multigene family containing several subfamilies. See Schiene at page 761, right Col., 1st paragraph. Regardless of the size of the gene family, Schiene was able to use the construct containing Ms-*rac1* in antisense orientation to successfully produce transgenic tobacco *rac1*-antisense plants. As described in Schiene, the antisense strategy was feasible because there exists a Rac-related protein coding sequence that is closely related to Ms-*rac1* in tobacco. See Schiene at page 768, left Col., last paragraph. As also described therein, some tobacco *rac* genes with lower homology to Ms-*rac1* remain uninfluenced by the antisense expression. *Id.* Thus, contrary to the Examiner's assertion, even if NADPH oxidases are encodes by a multigene family, one skill in the art would nevertheless have a reasonable expectation that antisense or sense suppression methodology would result in inhibited or reduced NADPH oxidase activity in plants as evidenced by Schiene.

For at least the above reasons, Applicants respectfully submit that the Patent Office has not met its burden to present evidence supporting the alleged unpredictability of using sense or antisense technology to reduce endogenous gene expression. Furthermore, as discussed in the Response dated December 15, 2009, the specification provides detailed guidance, including working examples, as to how to clone a cDNA encoding a NAPDH oxidase (Example 2), how to synthesize *in vitro* dsRNA of a NAPDH oxidase (Example 3), how to transiently transform dsRNA into a cell to create RNA interference (Example 4), and how to evaluate the pathogen resistance in the transformed cells (Example 4). The methodologies described in the specification are applicable not only to the full-length of SEQ ID NO: 1 as exemplified, but also any other sequences encoding NAPDH oxidases for which the reduction of protein quantity, activity or function is desired. Moreover, methodologies in using sense or antisense of a sequence in reducing quantity, activity or function of the encoded protein are within the knowledge of one skilled in the art as evidenced by Schiene. Thus, although some testing and

screening would be required when different methodology is used and/or different NAPDH oxidase genes or parts thereof are used, such testing and screening would not be extensive and is routine in nature, and thus, not undue. On these facts, an analysis under *In re Wands* supports enablement. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (routine screening of hybridomas was not "undue experimentation;" the involved experimentation can be considerable, so long as "routine").

In view of the present amendments, and further in view of the reasons already of record and the remarks provided above, Applicants respectfully submit that the art and the specification provide ample guidance and predictability for the present claims and the Examiner has not presented the evidence necessary to dispute the enablement provided in the instant specification. Accordingly, reconsideration and withdrawal of the enablement rejections is respectfully requested.

Written Description Rejection

Claims 1-23 further remain rejected for allegedly failing to comply with the written description requirement.

In maintaining the rejection, the Examiner again alleges that the claimed methods are not limited to the use of NADPH oxidase nucleic acid sequences. See Office Action at page 8. Without acquiescing to the merits of the Examiner's argument, claim 1 has been amended without prejudice or disclaimer to recite the claimed method with more specificity. As amended, claim 1 now requires that the reduction of NADPH oxidase content/activity/function is achieved by using a NADPH oxidase nucleic acid sequence (e.g. sense, antisense, or by RNAi approach). As stated by the Examiner, the specification describes the use of full-length NAPDH oxidase nucleic acids for reducing endogenous NADPH oxidase content/activity/function in a plant. See Office Action at page 8. Thus, Applicants believe that the present amendment clarifies the Examiner's concerns that the claims encompass the use of sequences other than NADPH oxidase nucleic acids.

In view of the present amendments, and further in view of the reasons already of record and the remarks provided above, Applicants respectfully submit that the specification provides

adequate written description for the claims as amended. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above remarks and further in view of the above amendments, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

This response is filed within the three-month period for response from the mailing of the Office Communication. No fee is believed due. However, if a fee is due, please charge our Deposit Account No. 03-2775, under Order No. 12810-00067-US from which the undersigned is authorized to draw.

Respectfully submitted,

By /Hui-Ju Wu/

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